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ORIGINAL RESEARCH ARTICLE

Effects and Costs of Hepatitis C Virus Elimination for the Whole Population in China: A Modelling Study

Meiyu Wu[1,2] · Jing Ma[3] · Sini Li[4] · Shuxia Qin[5] · Chongqing Tan[1,2] · Ouyang Xie[1,2] · Andong Li[1,2] · Aaron G. Lim[6,7] · Xiaomin Wan[1,2]

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Abstract

Background and Objective China has the highest number of hepatitis C virus (HCV) infections in the world. However, it is unclear what levels of screening and treatment are needed to achieve the WHO 2030 hepatitis C elimination targets. We aimed to evaluate the impact of scaling up interventions on the hepatitis C epidemic and determine how and at what cost these elimination targets could be achieved for the whole population in China.

Methods We developed a compartmental model incorporating HCV transmission, disease progression, and care cascade for the whole population in China, calibrated with data on demographics, injecting drug use, HCV prevalence, and treatments. Five different scenarios were evaluated for effects and costs for 2022–2030. All costs were converted to 2021 US dollar (USD) and discounted at an annual rate of 5%. One-way sensitivity analyses were conducted to assess the robustness of the model.

Results Under the status quo scenario, the incidence of hepatitis C is projected to increase from 60.39 (57.60–63.45) per 100,000 person-years in 2022 to 68.72 (65.3–73.97) per 100,000 person-years in 2030, and 2.52 million (1.94–3.07 million) infected patients are projected to die between 2022 and 2030, of which 0.76 (0.61–1.08) million will die due to hepatitis C. By increasing primary screening to 10%, conducting regular rescreening (annually for PWID and every 5 years for the general population) and treating 90% of patients diagnosed, the incidence would be reduced by 88.15% (86.61–89.45%) and hepatitis C-related mortality by 60.5% (52.62–65.54%) by 2030, compared with 2015 levels. This strategy would cost USD 52.78 (USD 43.93–58.53) billion.

Conclusions Without changes in HCV prevention and control policy, the disease burden of HCV in China will increase dramatically. To achieve the hepatitis C elimination targets, China needs to sufficiently scale up screening and treatment.

1 Introduction

Hepatitis C virus (HCV) is a blood-borne virus that is responsible for considerable morbidity and mortality. Globally, it is estimated that there are over 70 million individuals living with chronic hepatitis C, and around 400,000 people die annually from HCV-related cirrhosis or hepatocellular carcinoma (HCC) [1]. The introduction of highly efficacious direct-acting antivirals (DAAs) has dramatically changed hepatitis C treatment and made elimination of HCV a realistic public health goal [2]. As a result of these advances, the World Health Organization (WHO) has endorsed the Global Health Sector Strategy to eliminate HCV as a major public health threat by 2030, with targets to reduce new HCV infections by 80% and the number of HCV-related deaths by 65% compared with 2015 levels [3].

With an estimated about 10 million HCV infections in 2020, China has the largest number of HCV-infected people in the world, making it a key target country for global hepatitis C elimination [4]. The prevalence of HCV infection in the general population in China is 0.60%, which is lower than the prevalence of HCV infection in other high-risk groups [5]. Currently, injecting drug use is the main route of HCV transmission in China [6]. The HCV prevalence among people who inject drugs (PWID) is up to 67.0% (60.9–73.1%) [7]. However, less than one-third of HCV-infected individuals in China are aware of their infection status, and only 10% of these received treatment, leading to increasing hepatitis C-related morbidity and mortality [8]. Scaling up screening and treatment is therefore crucial to tackling the hepatitis C

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Key Points for Decision Makers

Without scale-up of screening and treatment, the incidence and mortality of hepatitis C would increase dramatically by 2030.

To achieve the elimination targets, an annual primary screening rate of 10% of unscreened population, with prioritization of high-risk groups, is needed to identify HCV infections, 90% of those diagnosed need to be treated, and regular rescreening is also needed to identify reinfections.

Scaling up treatment and screening to achieve hepatitis C elimination would cost $52.78 billion between 2022 and 2030, an average of $5.86 billion per year (0.50% of China's 2021 health expenditure of $1172 billion).

epidemic and achieving the target of hepatitis C elimination in China.

In 2019, DAAs were recommended as the first-line treatment strategy for hepatitis C by Chinese hepatitis C prevention and treatment guidelines [9]. In addition, China's national negotiation of drug prices has resulted in an average 85% price reduction for DAAs, with three DAAs now covered by national medical insurance [10]. These have laid a foundation for treatment scale-up; however, this scale-up depends on identifying infected individuals. Given the low diagnosis rate for hepatitis C in China, scaling up both screening and treatment to identify and cure patients with hepatitis C is essential to reduce the risk of HCV transmission and eliminate hepatitis C. However, it is unclear what levels of screening and linkage to care will be needed to achieve the target of hepatitis C elimination in China by 2030, as well as the associated costs. Therefore, this study aims to simulate different strategies to evaluate the effects and costs of hepatitis C elimination in China to determine what the levels of screening and treatment are required to reach the WHO target of hepatitis C elimination and what the associated costs will be.

2 Methods

2.1 Model Description

Based on a previous study by Lim et al. [11], we developed a HCV transmission compartmental model that incorporates HCV transmission, disease progression, and care cascades of hepatitis C for the whole population in China (Fig. S1). The model covers a time horizon from 1950 to 2030 and was developed using R software (R version 4.0.5; http://www.r-project.org). The population was divided into three age groups (young 0–19 years, young adult 20–34 years, and adult ≥ 35 years) to account for the age of initiation of injecting drug use and the variation of HCV prevalence in different age groups observed in the 2006 national HCV seroprevalence survey in China (ages 0–19: 0.18%, ages 20–34: 0.54%, and ages 35+: 0.69%) [12]. Individuals entered the model from the young category at a birth rate and are susceptible to HCV infection. As injecting drug use is currently the main route of HCV transmission in China [6], individuals were further divided into people who inject drugs (PWID), people who used to inject drugs (ex-PWID), and the general population (non-PWID) based on their risk behaviors as they aged. Susceptible individuals were infected at rates related to age, risk behavior, and hepatitis C prevalence. Infected patients would turn into the previously infected if there was spontaneous viral clearance or effective cure. Reinfection could occur in previously infected individuals. Chronic HCV infection could lead to varying degrees of liver fibrosis (F0–F3) and further progression to cirrhosis (F4), decompensated cirrhosis (DC), or HCC. Patients might die from advanced liver disease stages, and we attributed such deaths to HCV-related deaths. The care cascade refers to the series of services that hepatitis C patients receive as they move from diagnosis to treatment and ultimately to cure. Diagnosis of hepatitis C is based on HCV antibody (Ab) testing and RNA confirmation, and diagnosed patients are then initiated on treatment. We assumed that the risk of transmission of infected people who are aware of their infection status would be reduced by 50% (40–60%) [13], and that patients who failed to achieve sustained virologic response (SVR) after the initial treatment could be retreated up to 2 times at most (more details are described in Supplementary Material).

2.2 Model Parameters and Data Sources

Total population sizes, gender- and age-specific population sizes, and population growth rate were derived from the State Statistical Bureau of China and the United Nations Population Division [14, 15]. The data on the prevalence and injection-related mortality of PWID were obtained from published systematic reviews and observational studies [16–18]. Age-specific HCV antibody seroprevalence (anti-HCV prevalence) was derived from a national survey of hepatitis C in 2006 (0.43% overall) [12]. Data on hepatitis C-related disease progression and mortality were obtained from the published literatures [19, 20]. We calculated the total costs of screening, treatment, and disease management from the perspective of the Chinese healthcare system to assess the affordability of each strategy. The cost data were sourced from published studies [21, 22]. However, the costs associated with recruiting people for screening (such as general practice training or mass media campaigns) were not included in the model due to a lack of data. All costs were converted to 2021 US dollars (USD; $) based on an exchange rate ($1 = ¥6.45, September 2021) [23]. Costs were discounted at an annual rate of 5%. More details about model parameters are presented in Supplementary Material.

2.3 Model Calibration

A three-step calibration process was used for our model. Firstly, the average population growth rate was calibrated to fit the changes in total population size in China from 1950 to 2021 [14]. Following this, the age-specific mortality rates and the rate of individuals initiating injection were calibrated to fit the age distribution of the population in 2021 and the PWID prevalence [24, 25]. Finally, we incorporated the parameter sets obtained in the previous steps to calibrate the transmission coefficients, screening rate, and treatment rate to fit the anti-HCV prevalence in 2006, anti-HCV prevalence among PWID in 2010, as well as treatment numbers between 2009 and 2014 [12, 26]. Additionally, we externally validated the model by comparing the model outputs with other available data that were not used for modelling [27].

To reflect the uncertainty in the model parameters, for each step of the calibration process, parameter values were randomly sampled from uncertainty distributions, and unknown model parameters were then obtained by calibration using the least squares algorithm. The best-fitting unknown parameters were defined as those with the lowest goodness of fit (GOF) score. A total of 1000 parameter sets were generated and sorted in ascending order by GOF score. The top 100 parameter sets were used for subsequent analyses. Results are reported as medians and 95% uncertainty intervals (UI) from these model runs (details are provided in the Supplementary Material).

2.4 Scenario Analysis

We used the calibrated model to assess the impact of different levels of screening and treatment interventions under five scenarios in China from 2022. The status quo scenario assumes that the intervention remains at its current level, and four intervention scenarios were sequentially added to the status quo scenario according to their ambitiousness. Details of the scenarios are described in Table 1 and parameters for each scenario are shown in Table 2.

2.5 Outcomes

We evaluated the screening and treatment programs for hepatitis C based on cost consequences design. For each scenario, we reported HCV incidence, hepatitis C prevalence, and hepatitis C-related mortality from 2022 to 2030 and calculated the changes in incidence and mortality in 2030 compared with 2015 and 2022. To demonstrate the effect of the care cascade, we presented the proportion of people diagnosed and the proportion initiating treatment. In addition, we estimated the total cost of each scenario, incorporating screening costs (Ab testing and RNA testing), antiviral treatment costs, and chronic hepatitis C disease management costs. We also calculated the cost per cure by dividing the sum of screening and treatment costs by the total number of cured patients.

2.6 Sensitivity Analyses

Given the uncertainty in the model parameters, we conducted one-way sensitivity analyses for each intervention strategy to assess the impact of individual variables on the model results within a reasonable range, including incidence rates, disease management costs and total costs, and presented the results using tornado diagrams.

3 Results

The results of the calibration and validation are presented in Figure S2–9 in Supplementary Material. The anti-HCV prevalence of 0.98% (0.89–1.04%) in 2015 estimated by our model is within the range of 2015 anti-HCV prevalence estimated by experts [1.21% (0.93–1.49%)] [27]. Furthermore, our model estimated an overall HCV prevalence of 0.63% (0.60–0.72%) in 2015 that is close to the reported value of 0.7 (0.5–0.8%), which was obtained based on the expert estimate of anti-HCV prevalence [27].

Maintaining current levels of screening and treatment (SQ), the prevalence of HCV infection is projected to increase from 10.51 (95% UI: 10.08–11.92) million in 2022 to 13.09 (12.42–14.91) million in 2030 (Table 3). The incidence of hepatitis C is expected to increase from 60.39 (57.60–63.45) in 2022 to 68.72 (65.3–73.97) per 100,000 person-years in 2030, an increase of 20.27% (17.86–26.45%) compared with 2015. Between 2022 and 2030, there will be a cumulative 8.27 (7.83–8.75) million new infections and 2.52 (1.94–3.07) million deaths among infected patients, of which 0.76 (0.61–1.08) million will die from hepatitis C-related deaths and 1.76 (1.34–1.98) million will die from other causes (Fig. 1). By 2030, 23.54% (22.25–24.91%) of cumulative chronic HCV infections will be diagnosed, and 17.49% (14.45–17.95%) of diagnosed patients will be treated. The cascade of care for each scenario is shown in Fig. 2. The hepatitis C mortality will increase by 56.66% (45.08–60.55%) by 2030 compared with 2015 (Fig. 3).

Table 1 Intervention scenario details

Name (abbreviation)	Details
Status quo scenario (SQ)	This scenario assumes the intervention remains at its current level, with a calibrated annual primary screening rate of 5.56% (3.99–6.72%) and a calibrated annual treatment rate of 3.10% (2.45–3.27%) for patients diagnosed with HCV infection.
Strong scenario (SS)	This scenario assumes that a one-time random screening of 90% of the 2022 Chinese population will be completed by the end of 2030, in accordance with the WHO screening target [3]. This corresponds to an annual primary screening rate of 10%, with 80% of diagnosed infections initiating treatment.
Optimized strong scenario (OSS)	This scenario is similar to the strong scenario, but with a prioritization strategy, whereby PWID and individuals aged 35 years and older, who are considered to have higher prevalence and incidence of hepatitis C [4, 26], will be screened first, followed by the rest of population to achieve the annual screening quota.
Ambitious scenario (AmS)	This scenario adds rescreening interventions to the optimized strong scenario for individuals who were previously infected but cured and who were previously screened but not diagnosed, allowing for multiple screenings. Rescreening is performed every 10 years for the general population and annually for PWID, which is based on two previous studies [11, 33]. Notably, for individuals who were previously both Ab+ and RNA−, RNA testing is used directly for rescreening without the need for an Ab testing.
Aggressive scenario (AgS)	This scenario explores a more potential elimination scenario, which is an improvement on ambitious scenario, with rescreening of the general population every 5 years and 90% of diagnosed infections initiating treatment.

Table 2 Parameters for each scenario

Scenario	Primary screening rate for unscreened population	Rescreening rate for previously screened population		Initial treatment proportion for diagnosed patients
		General population	PWID	
Status quo scenario	5.56% (3.99–6.72%)	–	–	3.10% (2.45–3.27%)
Strong scenario	10%	–	–	80%
Optimized strong scenario	10%	–	–	80%
Ambitious scenario	10%	10%	100%	80%
Aggressive scenario	10%	20%	100%	90%

PWID, people who inject drugs

For the one-time random screening intervention scenario (SS), 27.48% (25.06–33.93%) of hepatitis C patients will be diagnosed and 80% (73.12–96.22%) of those diagnosed will be treated by 2030, avoiding 0.46 (0.39–0.6) million new infections and 184,066 (148,495–235,716) hepatitis C-related deaths and 130,387 (115,768–1463,470) non-hepatitis C related deaths compared with SQ. Incidence would increase by 10.46% (5.87–15.68%) and the HCV-related mortality would decrease by 0.56% (−2.49, 11.82%) from 2015 to 2030.

Compared with SS, the one-time screening but prioritization for PWID and people aged ≥ 35 years scenario (OSS) results in 1.49 (1.25–2.14) million more individuals being diagnosed and 1.21 (1.11–1.56) million more chronic infections being initially treated. By 2030, the incidence would increase by 2.61% (−4.6%, 6.74%), but the mortality would decrease by 16.65% (13.25–25.58%), compared with 2015 levels.

For AmS, the inclusion of the rescreening increases the number of people diagnosed and treated by 66.29% (60.0–89.14%) and 70.62% (53.39–81.59%), respectively, compared with OSS in 2022–2030. This results in a significant reduction of 70.73% (69.67–72.47%) in hepatitis C incidence and 38.42% (32.06–45.75%) in mortality by 2030 compared with 2015.

For AgS, which shortens the rescreening interval for the general population from every 10 years to every 5 years and increases the proportion of starting treatment from 80 to 90%, the number of diagnosed cases increases to 11.08 (10.64–12.5) million and the number of initial treatment to 10.37 (10.06–11.49) million by 2030. Compared with 2015 levels, hepatitis C incidence decreases by 88.15% (86.61–89.45%) and mortality decreases by 60.5% (52.62–65.54%) by 2030, and mortality continues to decrease to 65.60% of 2015 levels by 2031.

The disease management in the status quo scenario was estimated to cost a total of $26.39 billion over the

Table 3 Results of the baseline model

	Status quo scenario	Strong scenario	Optimized strong scenario	Ambitious scenario	Aggressive scenario
Prevalence of chronic infections					
Estimated total HCV infections in 2030 (millions)	13.09 (12.42–14.91)	10.23 (9.92–11.25)	8.86 (8.57–9.54)	4.07 (3.69–4.92)	1.88 (1.63–2.56)
Estimated HCV prevalence in 2030 (%)	0.93 (0.88–1.06)	0.72 (0.7–0.8)	0.63 (0.61–0.68)	0.29 (0.26–0.35)	0.13 (0.12–0.18)
Percentage change in prevalence by 2030 compared with 2022	+24.93 (+22.59 to +28.78)	−2.17 (−6.89 to +1.6)	−14.31 (−20.84 to −11.06)	−60.7 (−62.77 to −58.04)	−81.42 (−83.45 to −77.9)
Percentage change in prevalence by 2030 compared with 2015	+46.4 (+40.87 to +56.07)	+14.19 (+7.26 to +22.68)	+0.47 (−8.87 to +7.34)	−54.2 (−56.7 to −50.67)	−78.45 (−80.86 to −74.36)
Incidence of chronic infections					
Estimated cumulative incidence for 2022–2030 (millions)	8.27 (7.83–8.75)	7.81 (7.44–8.15)	7.32 (6.97–7.62)	4.2 (3.88–4.46)	3.23 (2.97–3.52)
Estimated HCV incidence in 2030 (per 100,000 person-years)	68.72 (65.3–73.97)	63.41 (60.67–67.08)	59.02 (55.12–61.84)	16.87 (15.14–17.83)	6.81 (5.8–7.97)
Percentage change in incidence by 2030 compared with 2022	+14.08 (+12.56 to +17.33)	+5.25 (+1.17 to +7.78)	−1.32 (−7.59 to +0.99)	−71.2 (−72.7 to −70.34)	−88.37 (−89.47 to −86.93)
Percentage change in incidence by 2030 compared with 2015	+20.27 (+17.86 to +26.45)	+10.46 (+5.87 to +15.68)	+2.61 (−4.6 to +6.74)	−70.73 (−72.47 to −69.67)	−88.15 (−89.45 to −86.61)
Deaths in infected group					
Estimated cumulative number of HCV- related deaths for 2022–2030 (millions)	0.76 (0.61–1.08)	0.58 (0.46–0.85)	0.54 (0.43–0.79)	0.49 (0.39–0.73)	0.4 (0.32–0.62)
Estimated HCV-related mortality in 2030 (per 100,000 person-years)	7.03 (5.62–9.91)	4.39 (3.52–6.37)	3.69 (3.01–5.34)	2.75 (2.28–4.22)	1.76 (1.47–2.94)
Estimated cumulative number of deaths from other causes for 2022–2030 (millions)	1.76 (1.34–1.98)	1.62 (1.22–1.84)	1.52 (1.14–1.69)	1.04 (0.83–1.17)	0.85 (0.68–0.96)
Percentage change in HCV-related mortality by 2030 compared with 2022	+37.59 (+33.09 to +39.52)	−12.59 (−18.77 to −10.93)	−26.69 (−31.41 to −24.13)	−46.03 (−49.97 to −41.73)	−65 (−68.05 to −59.21)
Percentage change in HCV-related mortality by 2030 compared with 2015	+56.66 (+45.08 to +60.55)	−0.56 (−11.82 to +2.49)*	−16.65 (−25.58 to −13.25)	−38.42 (−45.75 to −32.06)	−60.5 (−65.54 to −52.62)
Diagnosis and treatment					
Estimated cumulative number of chronic infections diagnosed for 2022–2030 (millions)	4.19 (3.97–4.42)	4.77 (4.37–5.92)	6.26 (5.62–8.06)	10.41 (10.02–11.84)	11.08 (10.64–12.5)

Table 3 (continued)

	Status quo scenario	Strong scenario	Optimized strong scenario	Ambitious scenario	Aggressive scenario
Percentage of chronic infections diagnosed by 2030[a]	39.86 (39.34–37.13)	45.58 (43.56–49.91)	59.85 (55.97–67.98)	99.56 (95.80–99.92)	106.58 (102.31–120.17)
Estimated cumulative number of treatments initiated for 2022–2030 (thousands)	741 (611–760)	3839 (3507–4615)	5048 (4616–6215)	8614 (8383–9534)	10374 (10067–11492)
Percentage of chronic infections treated by 2030[a]	7.05 (6.07–6.38)	36.65 (34.92–38.89)	48.23 (45.99–52.4)	82.39 (80.46–83.62)	99.75 (97.46–100.98)
Estimated cumulative number of cured for 2022–2030 (thousands)	742 (614–761)	3774 (3458–4519)	4947 (4544–6049)	8401 (8203–9268)	10173 (9925–11241)
Percentage of chronic infections cured by 2030[a]	7.06 (6.09–6.39)	36.04 (34.44–38.08)	47.27 (45.27–51.01)	80.35 (78.22–81.82)	97.81 (95.33–99.56)
Costs					
Total screening costs for 2022–2030 (billions)	0.83 (0.79–0.85)	1.24 (1.07–1.54)	1.99 (1.79–2.29)	5.39 (5.28–5.52)	8.52 (8.01–8.77)
Total treatment costs for 2022–2030 (billions)	1.3 (1.14–1.36)	7.06(6.07–8.2)	9.19 (7.9–10.93)	15.17 (14.15–16.59)	18.75 (17.41–20.5)
Total disease management costs for 2022–2030 (billions)	26.39 (14.54–31.12)	28.92 (17.34–35.27)	26.31 (16.37–32.6)	24.57 (16.32–29.93)	25.51 (17.81–31.13)
Total cost for 2022–2030 (billions)	28.51 (16.6–33.16)	37.21 (24.48–44.73)	37.5 (26.06–45.43)	45.13 (35.9–51)	52.78 (43.93–58.53)
Costs per cure	2856 (2771–3198)	2166 (2064–2271)	2215 (2132–2325)	2425 (2319–2551)	2645 (2499–2796)

[a]Compared with the number of chronic infections in 2022. The number of chronic infections in 2022 was estimated to be 10.51 (10.08–11.92) million, and the incidence was 60.39 (57.60–63.45) per 100,000 person-years, with an HCV-related mortality of 5.08 (4.05–7.27) per 100,000 person-years

*The confidence intervals reflect the inherent uncertainty in our estimates. The inclusion of negative bounds despite positive point estimates illustrates the variability and the possibility that the true effects may differ from the sample estimates. These ranges indicate that although the average effect estimated in the study suggests a reduction in mortality rates, there remains a possibility that the actual effect could be an increase

period 2022–2030. The other scenarios had lower disease management costs, with the AgS scenario being the lowest, at $0.88 billion less than the status quo scenario. Of all the five intervention scenarios, SQ would have the lowest median total cost of $28.51 ($16.6–$33.16) billion in 2022–2030. The estimated costs increase as screening and treatment scale up, and AgS has the highest total cost of $52.78 ($43.93–$58.53) billion. The costs of each scenario are shown in Fig. 4. For all scenarios, the cost per cure ranges from $2166 to $2856, with SS being the lowest. For AgS, which has the highest number of cured and costs, it costs $2645 per case cured.

The results of the sensitivity analyses are displayed in Figs. S12–14, where we show the top ten parameters that have an impact on the model results. Incidence rate was sensitive to spontaneous clearance rate, ceasing injecting drugs rate, and injecting-related death rate, changing within 10% of the baseline analysis results. The disease management cost parameters had a significant impact on the total disease management cost for all strategies as well as the total intervention cost. Total disease management costs could be reduced by 50% if management costs for all disease states were halved. In addition, total intervention costs were also sensitive to spontaneous clearance rate, DAA prices, and discount rates.

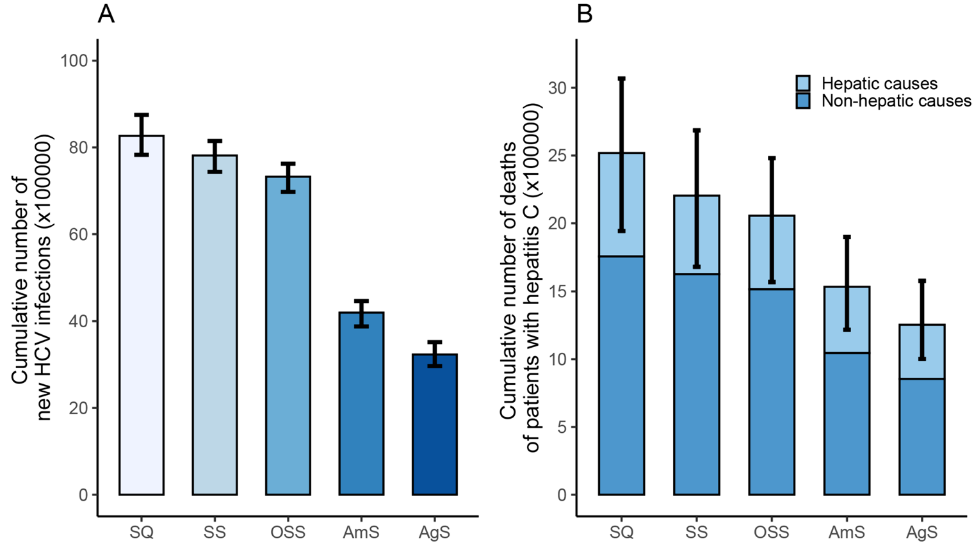

Fig. 1 Model-projected cumulative number of new HCV chronic infections and HCV-related deaths for each scenario between 2022 and 2030. Data are the median of 100 model runs, and the error bars indicate the 95% uncertainty interval. **A** Projected cumulative number of new HCV chronic infections. **B** Projected cumulative number of HCV-related deaths. SQ, status quo scenario; SS, strong scenario with an annual screening rate of 10% for the unscreened population, with 80% of diagnosed infections initiating treatment; OSS, optimized strong scenario, similar to SS, but with a prioritization strategy, whereby PWID and individuals aged 35 years and older will be screened first, followed by the rest of population to achieve the annual screening quota; AmS, ambitious scenario, OSS plus rescreening (every 10 years for the general population and annually for PWID). AgS, aggressive scenario, OSS plus rescreening (every 5 years for the general population and annually for PWID)

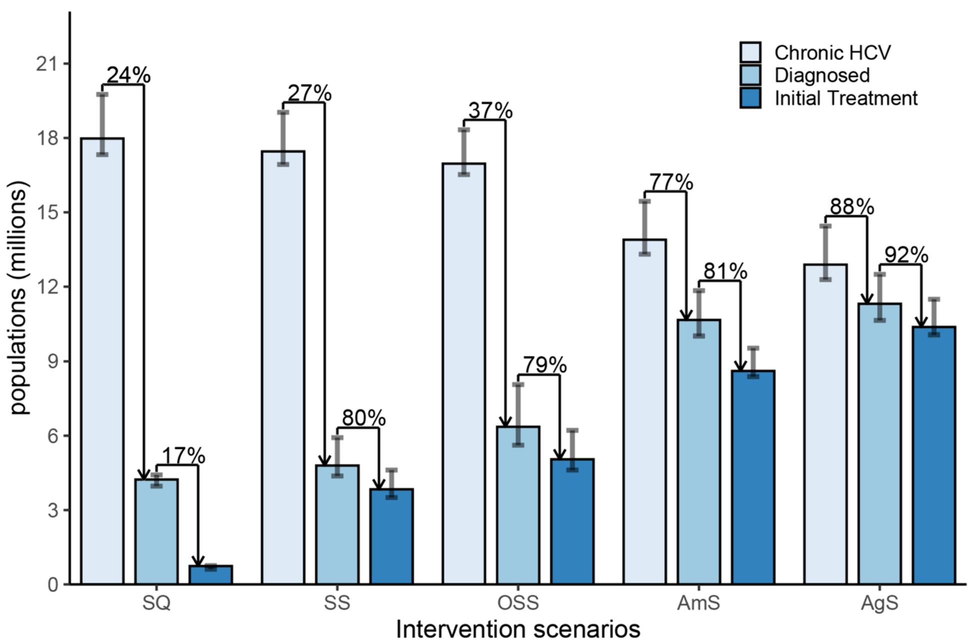

Fig. 2 Cascade of care for scenarios S1–S5. Data are the median of 100 model runs, and the error bars indicate the 95% uncertainty interval. For each scenario, the height of each bar represents the cumulative number of chronic HCV infections, diagnoses, and initial treatments by 2030, respectively. The arrows linking each bar indicate the proportion of the prior stage in the cascade of care that transitions to the subsequent stage. SQ, status quo scenario; SS, strong scenario with an annual screening rate of 10% for the unscreened population, with 80% of diagnosed infections initiating treatment; OSS, optimized strong scenario, similar to SS, but with a prioritization strategy, whereby PWID and individuals aged 35 years and older will be screened first, followed by the rest of population to achieve the annual screening quota; AmS, ambitious scenario, OSS plus rescreening (every 10 years for the general population and annually for PWID); AgS, aggressive scenario, OSS plus rescreening (every 5 years for the general population and annually for PWID)

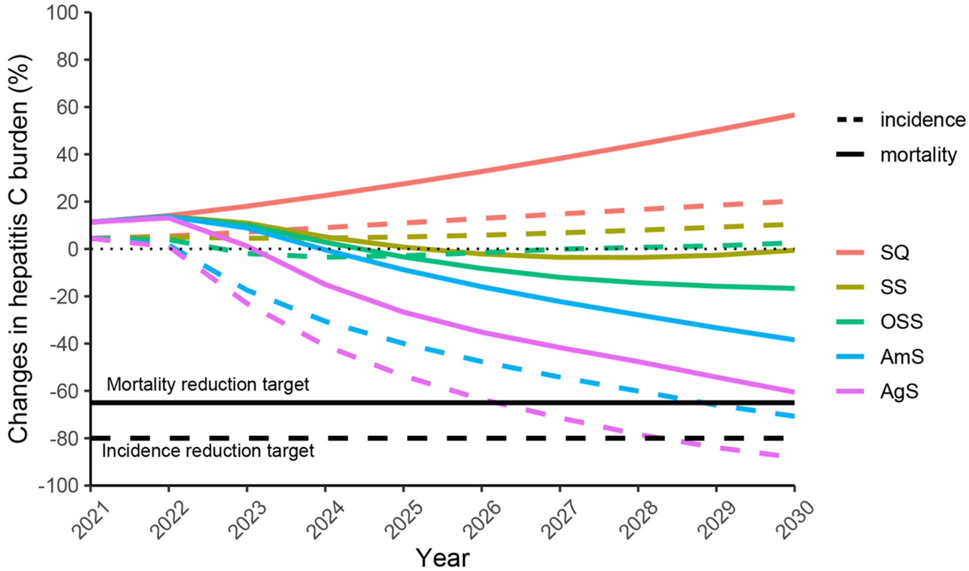

Fig. 3 Percentage changes in hepatitis C incidence and mortality achieved by 2030 compared with 2015 for each scenario. Data are the median of 100 model runs. The error bars indicate the 95% uncertainty interval. SQ, status quo scenario; SS, strong scenario with an annual screening rate of 10% for the unscreened population, with 80% of diagnosed infections initiating treatment; OSS, optimized strong scenario, similar to SS, but with a prioritization strategy, whereby PWID and individuals aged 35 years and older will be screened first, followed by the rest of population to achieve the annual screening quota; AmS, ambitious scenario, OSS plus rescreening (every 10 years for the general population and annually for PWID); AgS, aggressive scenario, OSS plus rescreening (every 5 years for the general population and annually for PWID)

4 Discussion

Our findings suggest that without scaling up screening and treatment, the hepatitis C incidence and mortality in China will increase by 20.27% and 56.66%, respectively, by 2030 compared with 2015. It could result in 2.52 million deaths among hepatitis C-infected patients during this period, with 0.76 million deaths from hepatitis C-related disease and 1.76 million deaths from other causes. By increasing the primary screening rate to 10%, conducting regular rescreening (annual for PWID, every 5 years for general population), and treating 90% of diagnosed patients, by 2030, China could reach the WHO target for incidence (an 80% reduction) and be very close to the target for mortality (a 65% reduction). Compared with the status quo, the aggressive strategy would avert about 5 million incidences and 1.2 million deaths, of which 0.3 million liver related deaths and 0.9 million non-liver related deaths. To achieve the goal, the total cost will be \$52.78 billion from 2022 to 2030, with annual costs of \$5.86 billion (0.50% of China's 2021 health expenditure, or \$1172 billion). The estimated cost per infection cured is \$2645, equivalent to 21.07% of China's GDP per capita in 2021 (\$12,554) [14, 28].

We found that the cost of disease management for achieving hepatitis C elimination would be lower than the status quo, but the total cost would be higher. This is similar to the results of the cost analyses in Myanmar and Indonesia [29, 30]. This may be attributed to the fact that in a country with a large population such as China, the population undergoing universal screening is much larger than that of patients with advanced liver disease, resulting in higher total costs. In addition, elimination costs associated with screening, antiviral treatment, and disease management are high in the short term. However, in the long term, these costs are expected to decline, yet the 9-year simulation period (2022–2030) in the model may be insufficient to capture the long-term economic benefits.

The results indicate that the cost of disease management is one of the key drivers in the total cost, reducing it could significantly reduce the economic burden in China. In addition, the test prices and DAAs drug prices are also key factors, so the Chinese government can negotiate special prices for the test kits and drugs to be used in the HCV elimination program, thus making it more affordable [31]. Our study results highlight the importance of HCV universal screening in China. It is true that a significant number of resources are required for universal screening and that China has the highest absolute number of HCV infections worldwide, but

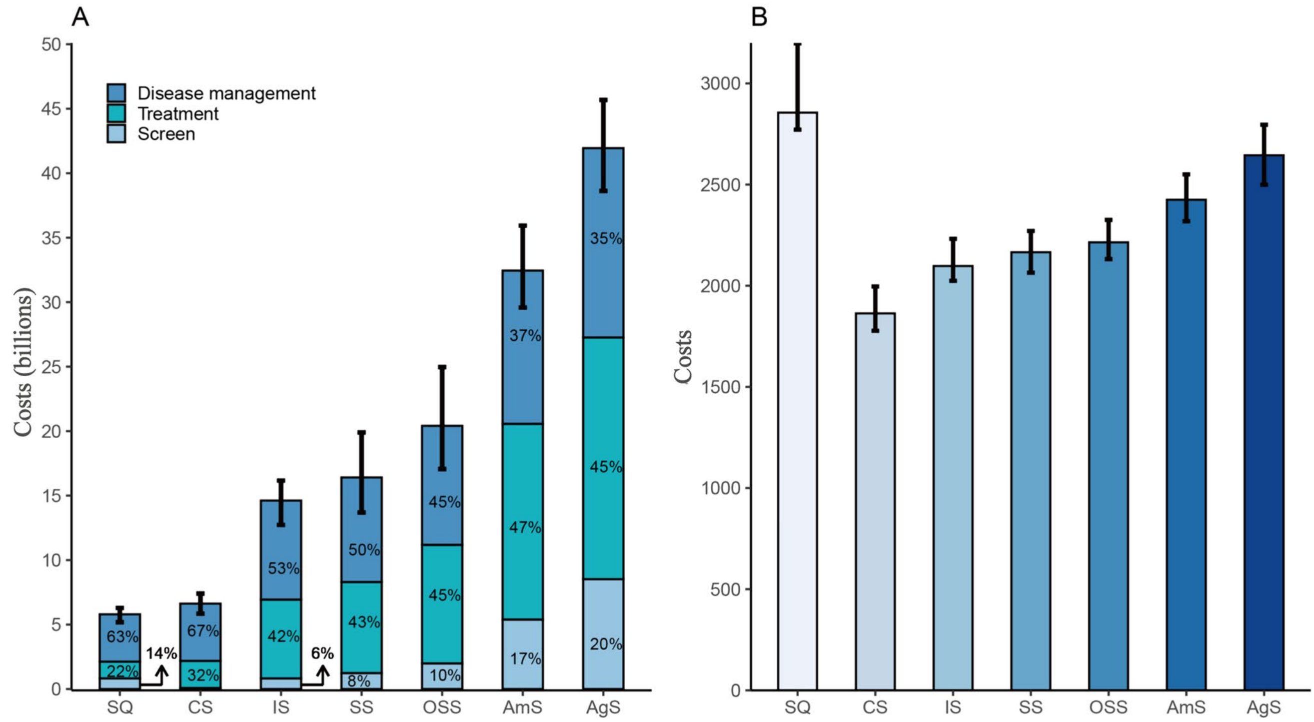

Fig. 4 Estimated costs for each scenario over 2022–2030. Data are the median of 100 model runs, and the error bars indicate the 95% uncertainty interval. **A** Total screening, treatment, and disease management costs. The internal values of the bars represent the proportion of total cost for each cost category. **B** Cost per cure. SQ, status quo scenario; SS, strong scenario with an annual screening rate of 10% for the unscreened population, with 80% of diagnosed infections initiating treatment; OSS, optimized strong scenario, similar to SS, but with a prioritization strategy, whereby PWID and individuals aged 35 years and older will be screened first, followed by the rest of population to achieve the annual screening quota; AmS, ambitious scenario, OSS plus rescreening (every 10 years for the general population and annually for PWID); AgS, aggressive scenario, OSS plus rescreening (every 5 years for the general population and annually for PWID)

the overall prevalence in the general population is relatively low. These may pose a challenge to the implementation of universal screening but it should not be seen as a complete barrier to implementation. In fact, the focus of China's future efforts is on the universal screening, diagnosis, and treatment of HCV within an integrated healthcare delivery system [32]. Moreover, universal screening has been proposed as an effective method in disease elimination [33, 34]. Although free screening programs targeting high-risk populations already exist in China, most incident HCV cases occur in the low-risk general population [35], thus recommending universal screening targeting the broader population. In addition to universal screening, targeted screening of the population of PWID is important, given the significantly higher transmission and prevalence rates of hepatitis C in this group compared with the general population. Moreover, the increased risk of reinfection among PWID requires more frequent screening interventions to more effectively identify HCV-infected individuals.

The aim of the study is to determine what levels of screening and treatment are needed to be scaled up by 2030 to achieve the HCV elimination in China, but it is also important to know how to achieve this scale-up. Scale-up in China will require the implementation of policy and financial incentives to increase screening rates, as well as addressing several key barriers, include improving individual awareness, willingness and ability to seek timely diagnosis and treatment, and improving access to services for hard-to-reach populations such as PWID [32, 36]. Overcoming these barriers requires a multipronged approach. First, an enhanced health education program should be implemented to improve health literacy and raise awareness of hepatitis C. Currently, China is actively enhancing health education related to hepatitis C prevention and treatment and improving health literacy to increase public awareness [37]. Second, an improved health security system is needed to reduce the financial risks associated with seeking diagnosis and treatment, with a particular focus on providing a safety net for those experiencing financial hardship [32]. Third, an integrated health care delivery system is required to facilitate easy access to timely screening, diagnosis, and treatment for those who are aware and willing [32]. In this context, the latest Chinese guidelines recommend HCV screening for all adults [4]. In addition, the healthcare sector has been working to simplify the pathway from diagnosis to treatment and to reduce the financial burden on patients with hepatitis C, thereby improving treatment adherence [38]. Lastly, a multifaceted approach should be used to improve access to services for hard-to-reach populations with hepatitis C, including training of PWID managers in government departments and addressing stigma and discrimination [36]. In China, the PWID managers mainly include the public security department, the health department, and the community. The management for the PWID population is usually arranged by the public security department to provide compulsory drug treatment in the community, referring to the mode of drug rehabilitation in which drug-addicted persons are forced to undergo medication, psychotherapy, and legal and moral education within a certain period of time by means of administrative measures [39, 40]. A comprehensive approach similar to China's "Four Free and One Care" policy for people living with human immunodeficiency virus (HIV) is needed to achieve scale-up of hepatitis C screening and treatment in China [41].

To our knowledge, this is the first study to construct a model incorporating the transmission of HCV, the natural history of the disease, and the care cascade to evaluate the effects and costs of hepatitis C elimination in China. As a country with the largest disease burdens of hepatitis C in the world, China is crucial to achieve the goal of global hepatitis C elimination. Our study suggests the levels of screening and treatment needed to eliminate hepatitis C in China and what public health effects can be achieved from these actions, providing evidence and reference for the government to develop a strategic plan for hepatitis C elimination. Improving hepatitis C prevention and control to eliminate hepatitis C requires a significant investment, and we have evaluated the budget using reliable cost data. These budget evaluations are important information to inform health policy and help to measure the affordability and feasibility of scaling up the screening and treatment for hepatitis C.

One study evaluated the health impact and return on investment of scaling up hepatitis C screening and treatment in Yunnan Province, China, but it only considered screening high-risk populations, not the whole population [42]. Although the overall HCV prevalence in the population is relatively low, the large population size results in a substantial number of infections. As a result, screening programs that target the entire population are necessary [43]. Another study used a microsimulation model to evaluate one-time random universal screening and treatment for all adults and estimate the budget needed to eliminate hepatitis C in China [35]. The health care costs in this study, however, were estimated using the WHO-CHOICE tool and US data, which means that the estimated budget may be inconsistent with the actual costs in the Chinese context. Our study improves on the previous analyses. First, based on a study that focused on Pakistan [11], we used a similar approach but with modifications to reflect the characteristics of the HCV burden in China. The validation results showed that our model's predicted epidemics were close to the available data. Furthermore, our model's results are expected to be even closer to actual data, as the expert estimate of the 2015 anti-HCV prevalence used for model validation may have overestimated the prevalence due to the reliance on studies conducted mainly in the adult population [44]. Second, we included both low- and high-risk individuals as the target population for screening and developed risk-based screening programs, which better reflect the characteristics of HCV transmission and distribution in China. Furthermore, we used reliable cost data from China, so that the estimated budgets are closer to actual costs needed to achieve hepatitis C elimination in China. Our findings indicate that with the most aggressive strategy, China will reach the incidence and mortality decrease targets by 2028 and 2031, respectively. Similarly, studies in other countries have also shown that significant scale-up of screening and treatment is needed to eliminate hepatitis C, with most countries reaching their targets by around 2030 [11, 29, 45, 46]. Our findings are consistent with our previous studies on Pakistan, where strong scenarios had minimal impact on mortality and incidence reduction targets [11, 47]. However, these results contrast with some earlier HCV elimination analyses conducted for China [35, 48]. This discrepancy may be attributed to significant differences from prior research in several key areas: the methods used for constructing the model, the model calibration, the data sources, and the underlying assumptions of the model.

4.1 Limitations

There are some limitations in our study. First, although injecting drug use has become the main route of HCV transmission in China, we did not include in the model other risk-based stratifications (such as dialysis) and coinfections [such as HIV and hepatitis B virus (HBV)], which affect HCV transmission and disease progression. Second, our model did not include liver transplantation for patients with advanced liver disease, but this is expected to have a small impact on the total cost of achieving HCV elimination because the number of HCV-related liver transplants performed in China is less than 250 cases per year at a cost of about $55,453 per case [21, 49–51]. Third, our cost analysis did not take into account staff costs, the cost of recruiting people and improving China's current healthcare infrastructure to provide large-scale screening and treatment for hepatitis C. Additionally, the disease management costs do not distinguish between cured, in-treatment, and untreated management costs due to a lack of data. Fourth, the use of coarse-grained age groups may not accurately reflect the true nature of the infected population and may mask differences within each group. Fifth, we did not conduct a cost-effectiveness analysis based on the results of the model and calculate the remaining quality-adjusted life expectancy from 2030. Finally, besides screening and treatment, preventive interventions like needle and syringe programs also contribute to reducing HCV transmission, but our model did not include the effect and cost of scaling up these preventive interventions due to a lack of available data in China.

5 Conclusion

In conclusion, by using a calibrated HCV transmission compartmental model to evaluate different screening and treatment strategies for hepatitis C, our study suggests that if the status quo continues, the incidence and mortality of hepatitis C will increase substantially in China by 2030. Achieving the target of hepatitis C elimination in China requires extensive scale-up of screening and treatment and a substantial investment of $5.86 billion per year.

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Declarations

Competing Interests The authors declare that they have no competing interests.

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Patient and Public Involvement Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

Patient Consent for Publication Not applicable.

Ethics Approval Not applicable.

Data Availability Statement All data relevant to the study are included in the article or uploaded as online supplemental information.

Code Availability The code associated with this study is proprietary.

Author Contributions M.W., J.M., S.L., and X.W. developed the model and performed the analyses and interpreted the results. M.W., S.Q., O.X., and A.n.L. collected data and drafted the manuscript. A.L. and X.W. contributed to the conception and design of the primary model. M.W., C.T., and X.W. had access to and verified the data. M.W., A.L., and X.W. were responsible for the decision to submit the manuscript. All authors have read and approved the final article.

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Authors and Affiliations

Meiyu Wu[1,2] · Jing Ma[3] · Sini Li[4] · Shuxia Qin[5] · Chongqing Tan[1,2] · Ouyang Xie[1,2] · Andong Li[1,2] · Aaron G. Lim[6,7] · Xiaomin Wan[1,2]

✉ Aaron G. Lim
aaron.lim@bristol.ac.uk

✉ Xiaomin Wan
wanxiaomin@csu.edu.cn

[1] Department of Pharmacy, The Second Xiangya Hospital, Central South University, 139 Renmin Rd, Changsha 410011, Hunan, China

[2] Institute of Clinical Pharmacy, Central South University, Changsha 410011, Hunan, China

[3] Department of Gastroenterology, The Second Xiangya Hospital, Central South University, Changsha 410011, Hunan, China

[4] The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China

[5] Department of Pharmacy, The First Affiliated Hospital of Guangxi Medical University, Nanning 530021, Guangxi, China

[6] Bristol Medical School, Population Health Sciences, University of Bristol, Bristol, UK

[7] Bristol Medical School, Population Health Sciences, University of Bristol, Oakfield House, Oakfield Grove, Clifton BS8 2BN, UK